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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,446	07/13/2006	Beat Weber	753-61 PCT/US	9882
23869	7590	03/05/2007	EXAMINER	
HOFFMANN & BARON, LLP 6900 JERICHO TURNPIKE SYOSSET, NY 11791			O DELL, DAVID K	
		ART UNIT	PAPER NUMBER	
		1609		
SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE		DELIVERY MODE	
3 MONTHS	03/05/2007		PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,446	WEBER ET AL.	
	Examiner	Art Unit	
	David K. O'Dell	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 January 2006.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-18 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-18 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-18 are pending in the application.
2. This application is the National Stage of International Application No.

PCT/CH2004/000408, filed June 29, 2004, which claims the benefit of CH 1274/03, filed July 21, 2003.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 14 & 16 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of Pd catalysts, it does not reasonably provide enablement for the exhaustive list of metals/complexes so claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claim 14 recites that the dehydrogenation catalyst is "selected from amongst compounds (salts and complexes) of the transition metals of the periodic system, preferably from compounds of the metals of Group VIII elements, in particular from iron, ruthenium and osmium; cobalt, rhodium, and iridium; nickel, palladium and platinum; copper, silver and gold preferably from compounds based on rhodium, palladium and platinum." None of these compounds have been shown to promote the reaction of the process in claim 1, except a handful of Pd complexes. The nature of the

catalyst is essential to the reaction and the selection is critical. While applicant considers this reaction a dehydrogenation, it is better viewed as dehydrosilylation or in one case a dehydrocarbonylation. While the mechanism is not known with certainty, this is homogenous catalysis and the substrate must intimately interact with the catalyst in an ordered fashion. Tsuji, has proposed a mechanism for these reactions in his paper *Tetrahedron Letters* 1984, 25, 4783, where some of the reactions used in this application were revealed for the first time. Pd is peculiar in that it has the remarkable ability to shuffle between the 0 and +2 oxidation state readily, making complexes of Pd the only known catalysts for this reaction. Claim 16 recites using a diamine ligand to affect "thermal stabilisation" no evidence is provided that such an addition would stabilize the catalyst.

4. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for one example (and possibly other alkyl) does not reasonably provide enablement for the exhaustive list of substituents given. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. While applicant has provided for the preparation of a handful of silyl ketene aminals, the scope of what is claimed does not enable one to practice the invention as claimed. For example, amides are well known to undergo both N- or C-silylation as well as O-silylation and under the conditions given it has been shown that for certain substrates under the scope of the claims, C-silylation will occur (Bergmann, H. J.; Maryhofer, R.; Otto, H. H. *Archive der Pharmazie (Weinheim)* 1986, 319, 203

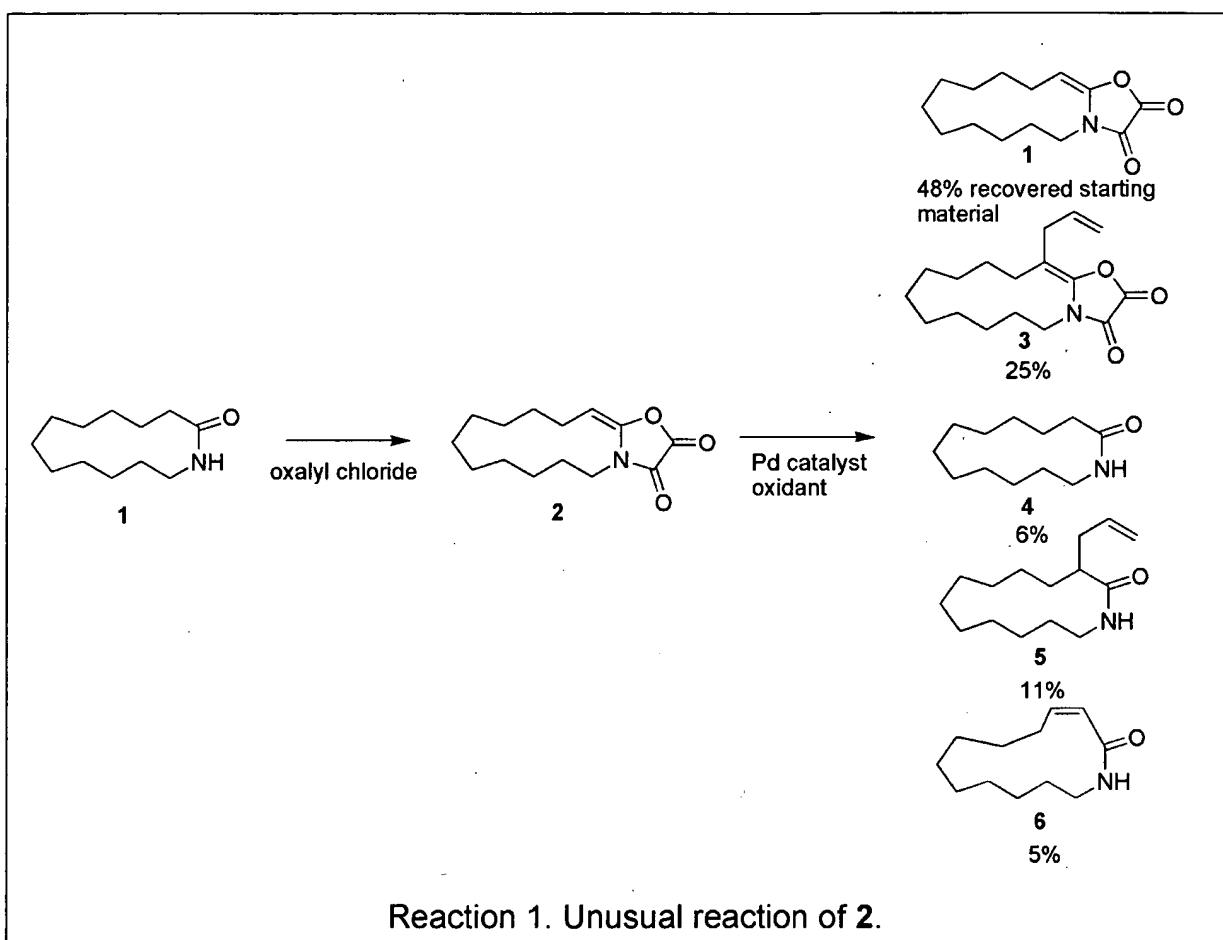
abstract provided). The C-silylated species have never been shown to undergo this reaction. Where R₃ is H, then N-silylation can occur (Thomas, E. J.; Whitehead, J. W. *F. J. Chem.Soc. Perkin Trans. 1* **1989**, 507). The N-silylated species have never been shown to undergo this reaction either. Thus applicants conditions cannot be used to prepare the substrates required for the scope of the claims. As per MPEP:

A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. **The same can be said if certain chemicals are required to make a compound or practice a chemical process.** *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981). (emphasis added)

The examiner finds the oxidation of the vinylidene 1,3-oxazol-2,3-dione **2**, with Pd/oxidants (Reaction 1) incredulous. While the Merck Patent (EP-A-0 478 366) states that an amine base is necessary applicants have omitted this step, and one can only wonder where the 2 equivalents of HCl generated from oxallyl chloride went. In applicants ¹³C NMR the methine carbon of the exocyclic double bond of **2** appears to be absent, so the correct identification may be in question. It is not clear what the applicant

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hoped to accomplish by reacting **2** in the same fashion as the silyl ketene aminals, but the product mixtures are extremely complex.



It is likely that what applicant has described as compound **2** is in fact the hydrochloride salt. Product **5** can be seen as arising from coupling of the starting material with decarboxylated allyl carbonate as described by Tsuji et. al. *Tetrahedron Letters* 1984, 25, 4783, which is expected. The production of **3** could be rationalized mechanistically, but such discussion is not appropriate here. For **6** the tenuous identification on MS data alone is questionable. It seems very likely that the product described as **6** is actually a mixture of regioisomeric olefins (i.e. 3,4,5,6 double bond etc.), since Pd is well

known to promote such isomerizations (Harrod, J. F.; Chalk, A. J. *J. Am. Chem. Soc.* 1964, 86, 1776). The aforementioned questionability of the identity of the starting material 2 and its likelihood of being contaminated with large amounts of HCl add to the problem and are a likely culprit for the production of 4. No data has been provided for 4, but it should have been compared to an authentic sample. The product 6, which is the desired product, is analogous to the reaction described by Minami, et. al. *Tetrahedron* 1986, 42, 2971-2977, pg. 2974 column 2, which employs the vinyl acetates as substrates. The applicants may need to add Bu₃SnOMe in order to accomplish the transformation. Applicants transformation is of course not catalytic. Regardless, the low yield and the absence of more working examples fail to enable this transformation for the scope as claimed.

The factors outlined in *In Re Wands* are appropriate, and in particular, As per the MPEP 2164.01 (a): "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification , at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright* 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." It is very clear that one could not make/use this very broad invention that has few working examples in this unpredictable art without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: Formula III has been omitted from the claims and one would have difficulty ascertaining its structure.

6. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case the method of claim 1 step (C) recites "optionally removing, if present, the protective group R8". The group R8 is removed in every case in the instant invention and there is no case where it is an optional substituent, or optionally removed. The concomitant removal of R8 defines the process as disclosed (i.e. dehydrosilylation (loss of HSiR₃ where R8 is SiR₃) or dehydrocarbonylation where R₈ is carbonyl etc.). The process has been examined as that of the wider disclosure although that is not what has been claimed.

Claim Rejections – Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-18 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim of copending Application No. 10/521,421. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed process embraces the process claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 18 is rejected under 35 U.S.C. 102(b) as anticipated by Weisgerber et. al. U.S. Patent 2,535,245. Acrylamide, a compound of claim 1, was disclosed therein.

Claim Rejections – 35 USC § 103

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

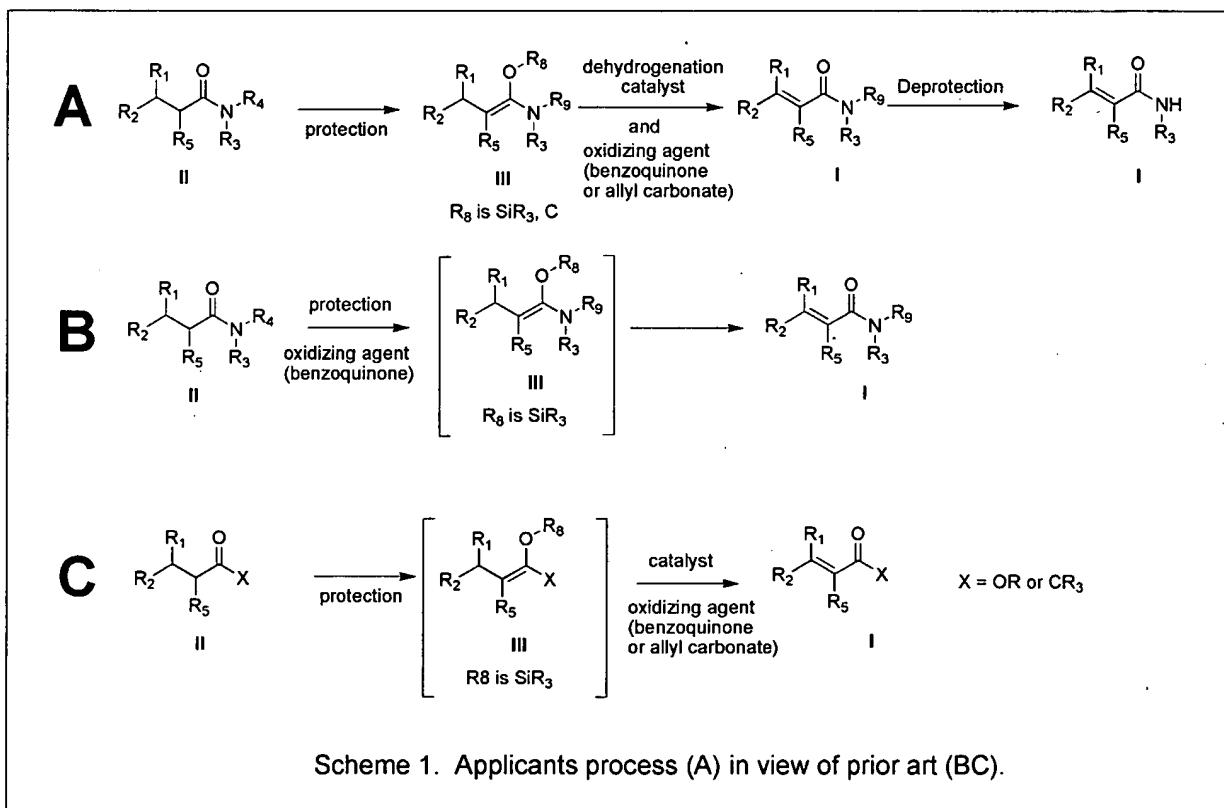
10. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhattacharya et. al. U.S. Patent 5,084,574 in view of Minami et. al. *Tetrahedron* 1986, 42, 2971 and Ito et. al. *J. Org. Chem* 1978, 43, 1011. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- A) Determining the scope and contents of the prior art.
- B) Ascertaining the differences between the prior art and the claims at issue.
- C) Resolving the level of ordinary skill in the pertinent art.
- D) Considering objective evidence present in the application indicating obviousness or nonobviousness.

- A) The prior art of Bhattacharya et. al. teaches that silyl ketene aminals can be oxidized to α - β unsaturated amides with quinone based oxidants, including benzoquinone, DDQ, and others. This reaction can be viewed as a dehydrosilylation. Ito et. al. teach that silyl enol ethers derived from ketones are oxidized to α - β unsaturated ketones with Pd catalysts and a quinone co-oxidant. Furthermore, Minami et. al. teach that silyl ketene acetals are oxidized by Pd catalysts to α - β unsaturated esters, and that the reaction can be made catalytic by the use of allyl carbonates.
- B) The difference in the claims at issue and the prior art are graphically illustrated in Scheme 1. Claim 1 from which all the other rejected claims depend (2-17) recites

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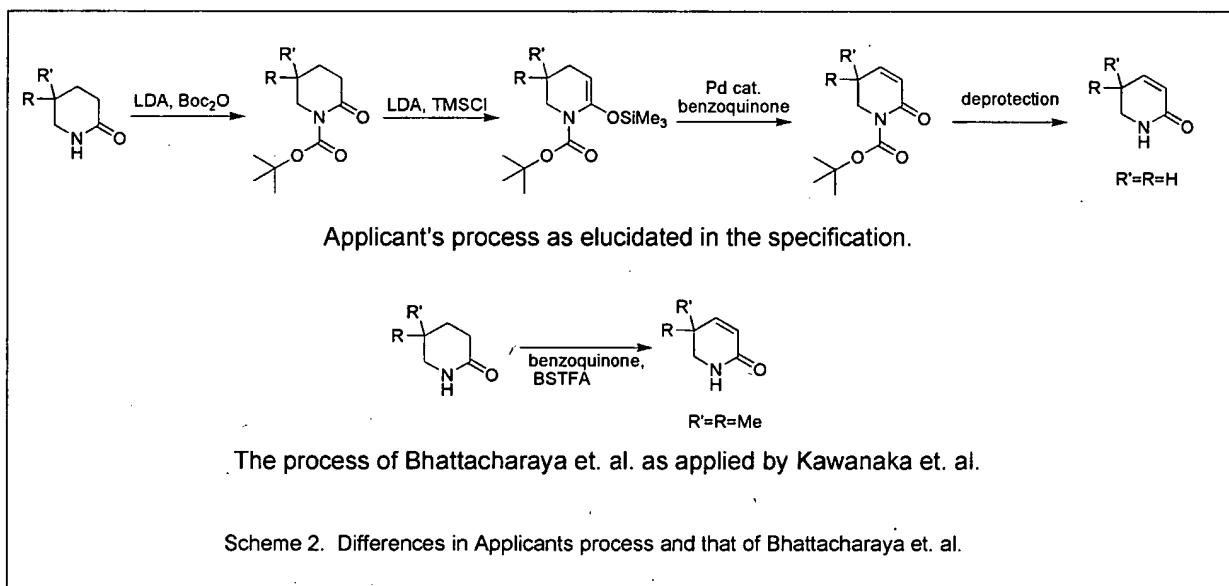
"reacting compounds of the general formula (II).....to produce a compound of the general formula III...reacting " III " in the presence of a dehydrogenation catalyst and" "an oxidising agent, such as optionally substituted benzoquinone, allyl methyl carbonate..." and removal of protective groups. This is graphically illustrated as **A**. The process of Bhattacharya et. al., is shown in reaction **B**. The processes of Minami et. al. and Ito et. al. are shown as **C**.



The process of the instant invention (**A**, where R_8 is SiR_3) differs from the process of Bhattacharya et. al. (**B**), in that everything has been conducted in one pot and no hydrogenation catalyst is necessary. In this case the reagent bis(trimethylsilyl)trifluoroacetamide (BSTFA) selectively forms a TMS ether in-situ, as has been shown in mechanistic studies (Bhattacharya et. al. *J. Am. Chem. Soc.* 1988,

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110, 3318). This TMS ether then undergoes subsequent benzoquinone mediated dehydrosilylation. Applicant's process has used multiple steps to form the TMS ether in a conventional manner (N-protection, LDA, TMSCl), which is the same reactive intermediate in the process of Bhattacharya. As illustrated in Scheme 2, the Bhattacharya process has been used by Kawanaka et. al. (*Bioorg. Med. Chem. Lett.* 2002, 12, 2291) to prepare essentially the same product ($R' = Me$) that applicant has as an example in the disclosure ($R' = H$).



In addition to applicant's alternate route to form a TMS ether, applicant has added a Pd catalyst to the reaction. It does not appear to be necessary in this case as benzoquinones themselves can mediate the dehydrosilylation without a catalyst.

Applicant's process can also be viewed as an obvious variation of the work of Ito et. al. and Mianmi et. al. Applicant has recited reaction conditions exactly as those disclosed by both processes. The process of Ito uses Pd catalysts and a benzoquinone co-oxidant, while Minami et. al. employs Pd catalysts and allyl carbonates. In the case

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of Ito, X is CR₃ (Scheme 1, C). In the case of Minami, X may be OR or CR₃. Applicant has simply changed X to NR₂. Since the moiety X is not actively involved in the process or undergoing transformation, it can be viewed as a spectator group. The use of amides necessitates the protection/deprotection sequence in order to form the desired silyl ketene aminals and would have been obvious to one of ordinary skill in the art.

C) The level of ordinary skill in the art is high. Those who conduct and design organic syntheses typically have Ph.D.'s and years of experience and are aware of methods to introduce double bonds α to carbonyls. While there are a myriad of ways to achieve this transformation (phenylselenation/oxidative elimination, etc.) one would immediately recognize that the transformations of Minami and Ito could be applied to silyl ketene aminals as well as other compounds (silyl ketene thioacetals for instance). The opinion set forth in *In re Surrey et. al.* (CCPA 1963) 319 F2d 233, 138 USPQ 67 is illustrative of the reasoning here:

Mere novelty of one of the reactants does not render an otherwise conventional chemical process patentable, since it does not impart anything to process which is unobvious to one skilled in the art; it constitutes no more than an obvious application of old process to new compounds; from point of view of chemical reaction and reactive groups concerned, same reaction takes place.

The opinion set forth in *In re Larsen* (CCPA 1961) 292 F2d 531, 130 USPQ 209 is also relevant :

A case in point is *Wirebounds Patents Co. et al. v. H.R. Gibbons Box Co.*, 25 F.2d 363 (CCA 7th Circuit). In holding the method claims there involved unpatentable, the court said: Moreover, the method patent contains nothing but the natural and obvious method of producing the box. It cannot be considered invention to describe and claim a process, or to produce a machine, or formulate a method which any successful mechanic would produce when required to effectuate a given result. The process claims

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define, in effect, only the reaction of A with B to produce AB, the reaction admittedly being old except for the selection of A and B from the mass of known materials available. Though they point out novel subject matter, these claims, tested against the prior art, do not define anything unobvious to one of ordinary skill in this art.

This art is chemistry. Were we in a mechanical art, I think no one would trouble to argue that every time a new tool or machine is invented one can obtain process claims directed to nothing more than the obvious steps of selecting the materials, forming the parts on suitable machines, and assembling them in their operative relationship. I can see no distinction in principle here. Yet that is what applicant contends in advancing in his conclusion. (emphasis added)

It is therefore submitted that the claims are properly rejected as unpatentable over what is already known in the art, and that they recite no more than the obvious variation of an old reaction.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571) 272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang who can be reached at (571)-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cecilia Tsang
CECILIA TSANG
SPE, TCI 1609